REMARKS

I. Status of the Claims

Claims 1-5, 35, 36, 39-42, 44, 50, 51, 54-57, and 59 are under consideration in this application. Claims 6-34, 37, 38, 43, 45-49, 52, 53, and 58 were withdrawn from consideration by the Examiner as being directed to non-elected subject matter. Claims 1-5, 35, 36, 39-42, 44, 50, 51, and 54-57 are amended. Claims 1-5, 35-36, 39-42, 50-51, and 54-57 are amended by deleting the words "the" or "the general" before formula. Claims 1-5, 35-36, 39-42, 50-51, and 54-57 are also amended to recite "a pharmaceutically acceptable salt thereof" instead of "its pharmaceutically acceptable salt thereof." New dependent claim 59 is added. Support for claim 59 may be found, for example, on page 35, line 16 to page 36, line 22, and on page 47, lines 10-15, of the as-filed specification.

II. Opposition in Related Foreign Application

Applicants were informed on January 2, 2007, that an opposition had been filed in Chile against a related application. The opponent asserted art cited in the International Search Report, which was submitted to this Office in an IDS filed October 28, 2003. While Applicants disagree that the asserted art anticipated Applicants' claims, Applicants amended the claims of the related Chilean application to proviso out four compounds, 5-fluorocytidine, 3'-deoxycytidine, 2'-deoxycytidine, and 5-hydroxyuridine, that were claimed for use in the manufacture of a medicament for the treatment or prophylaxis of a host exhibiting abnormal cellular proliferation. Even though the claims that were amended in Chile are currently withdrawn in this application, Applicants believe that the subject matter is relevant to the claims currently

under examination. Therefore, Applicants voluntarily amend claim 1 to exclude the use of 5-fluorocytidine, 3'-deoxycytidine, 2'-deoxycytidine, and 5-hydroxyuridine for the treatment of a host having abnormal cellular proliferation. Claims 39 and 41 are likewise amended to delete the phrase "abnormal cellular proliferation."

III. Restriction Requirement

After considering Applicants' reply filed on October 19, 2006, the Examiner has reduced the number of groups subject to the Restriction Requirement from 71 to 11 as set forth on pages 2 and 3 of the Office Action. Applicants have previously elected Group I with traverse. In this Office Action, new Group I includes claims 1-5, 35-36, 39-42, 44, 50-51, and 54-57. Applicants continue to respectfully traverse.

M.P.E.P. § 803 states that two requirements must be met before a proper Restriction Requirement may be made. These two requirements are: "[t]he inventions must be independent . . . or distinct as claimed; and there would be a serious burden on the Examiner if restriction is not required . . . ." (Emphasis added). The Examiner fails to establish the second requirement set forth in M.P.E.P. § 803, that a serious burden on the Examiner exists if restriction is not required among Applicants' claims. M.P.E.P. § 808.02 lays out the requirements for establishing a serious burden. An examiner must show that the search and examination would impose a serious burden on the Office because the alleged inventions have a separate classification, a separate status in the art, or a different field of search. *Id.*

Here, the Examiner has still not demonstrated how the search of the formulas or species of the withdrawn claims would place an undue burden on him. Applicants again emphasize that all of the compounds used in the claimed methods are nucleosides

containing a narrow group of bases. Applicants should not be penalized for disclosing particular formulas of a genus that differ by nucleoside base or the presence of a bond connecting the base to the sugar moiety. In addition, the presence of a double bond or the substitution of one atom in the sugar moiety should also not place an undue burden on the Examiner.

Moreover, the Examiner rejects Applicants' argument that Original Group LXIV (claims 30 and 45), Original Group LXV (claims 31 and 46), Original Group LXVI (claims 32-34 and 47-49), and Original Group LXXI (claims 43 and 53) should be rejoined with Group I. The Examiner asserts that those compounds are outside the scope of those claimed in claim 1. Office Action at page 3. Applicants respectfully traverse.

The Examiner provides no basis for concluding that it would be a serious burden to search the formulas or species of claims 30-34 and 45-49 (New Group X) along with the formulas of claim 1. While claim 1 does not specifically encompass compounds containing the OP^2 moiety in the 2'-position, as recited in claim 30, for example, claim 1 does recite compounds containing OH and OCH_3 substituents in the 2'-position. Moreover, despite this difference in substitution at the 2'-position, the subject matter of New Group X is still within the same field of search and classification as the elected New Group I. Therefore, the Examiner fails to establish that a serious burden exists if restriction is not required between the claims in elected New Group I and New Group X. As such, Applicants respectfully request the rejoinder of claims 30-34 and 47-49 with New Group I.

IV. Claim Objection

The Examiner objects to claim 1 since it contains multiple periods. Office Action at page 4. Claim 1 is amended to delete the multiple periods, rendering this objection moot.

V. Rejection Under 35 U.S.C. § 112

The Examiner rejects claims 1-5, 35-36, 39-42, 44, 50-51, and 54-57 under 35 U.S.C. § 112, first paragraph. According to the Examiner, the specification "while being enabling for treatment of *Flaviviridae*, *Orthomyxoviridae*, or *Paramyxoviridae* viral infections, or abnormal cellular proliferation, does not reasonably provide enablement for prevention of the same." Office Action at page 4. Applicants respectfully disagree with the Examiner. Solely in order to expedite prosecution, Applicants have amended the independent claims to delete "or prophylaxis." Applicants submit that this amendment renders the rejection for alleged non-enablement moot and respectfully request that the rejection be withdrawn.

The Examiner rejects claims 1-5, 35-36, 39-42, 44, 50-51, and 54-57 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

According to the Examiner, claim 1 is indefinite for reciting administering an effective amount of a compound of formula (I) or (II), but defining formulas [I-a], [I-b], [I-c], [II-a], [II-b], and [II-c]. *Id.* at 7. Claim 1 is amended to recite administering "an effective amount of a compound of formula [I-a], [I-b], [I-c], [II-a], [II-b], or [II-c]." Accordingly, this rejection is now moot.

The Examiner also rejects claim 1 as allegedly indefinite for defining various variables with the use of a parenthesis, "such as X^1 and X^2 for example, as optionally being halogen (F, Cl, Br, or I)." *Id.* at 8. Claim 1 is amended to delete "halogen" and the parentheses so that only F, Cl, Br, and I are recited. Applicants respectfully request that this rejection be withdrawn.

The Examiner also contends that claim 1 is indefinite because the definitions of R^2 and $R^{2'}$ and R^3 and $R^{3'}$ are not proper Markush language. *Id.* at 8. Claim 1 is amended to use proper Markush language in defining all substituents. Therefore, this rejection is now moot.

The Examiner further rejects claim 1 as allegedly indefinite since the claim provides that R^4, $R^{4'}$, etc., are independently arylalkyl "such as unsubstituted or substituted phenyl or benzyl." *Id.* at 8. Applicants delete the phrase "such as unsubstituted or substituted phenyl or benzyl" and add the subject matter in new dependent claim 59. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The Examiner rejects dependent claim 2 as lacking an antecedent basis for "the limitations that R^1 and $R^{1'}$ are D, or R^2 or R^3 are O-Ms in the table." *Id.* at 8. The Examiner also advises Applicants to ensure that all of the variables in the table have support in the claims from which they depend. Claim 3 is similarly rejected by the Examiner as lacking an antecedent basis for the limitation that $R^{3'}$ is O-Ac in the table. *Id.* The amended claims recite no variables that are not recited by independent claim 1. Therefore, Applicants respectfully request that these rejections be withdrawn.

The Examiner rejects claims 4 and 5 as allegedly indefinite for providing that various compounds have F in the R^2 position but "according to claim 1, that 'at least one of R^2 and $R^{2'}$ is H' and since claims 4 and 5 are drawn to compounds only comprising the moiety R^2, that this cannot be F." *Id.* at 9. Applicants have amended claim 1 to recite "such that for the nucleoside of the general formula (I-a), (I-b), and (I-c) at least one of R^2 and $R^{2'}$ is hydrogen and at least one of R^3 and $R^{3'}$ is hydrogen" since only compounds of the general formula (I-a), (I-b), and (I-c) have both R^2 and $R^{2'}$ and R^3 and $R^{3'}$ substituents. Because claims 4 and 5 recite compounds of formulas (II-a) and (II-b), respectively, Applicants submit that the amendment to claim 1 renders this rejection moot.

The Examiner asserts that claims 1, 35-36, 39-42, 44, 50-51, and 54-57 are indefinite since those claims fail to state to whom the compound is administered. *Id.* at 9. These claims are amended to recite "to a host in need thereof." Accordingly, Applicants respectfully request that this amendment be withdrawn.

The Examiner also rejects claims 1, 35-36, 39-42, 44, 50-51, and 54-57 as allegedly indefinite for using the phrase "treatment or prophylaxis of a host exhibiting a viral infection or abnormal cellular proliferation." *Id.* at 9. The Examiner asserts that it is unclear whether the hosts actually have the claimed diseases or just exhibit them. *Id.* Solely to further prosecution, Applicants have amended these claims to recite "having" instead of "exhibiting." Applicants respectfully request that this rejection be withdrawn.

The Examiner rejects claims 35-36 and claims 50-51 as allegedly indefinite for reciting "its β-L enantiomer" since the compound is already in its β-L form. *Id.* at 9-10. Applicants have amended claims 35-36 and 50-51 to recite "or its β-D enantiomer." The

Examiner also alleges that claims 50-51 are indefinite since those claims are drawn to using a β-D nucleoside of formula XXII but are depicted in their β-L form. Applicants have amended claims 50-51 to recite "or a β-L nucleoside of the formula . . . ." Therefore, Applicants respectfully submit that these rejections are now moot.

The Examiner also rejects claims 35-36 and 50-51 as allegedly indefinite for stating that various variables are "the same as defined previously." *Id.* at 9. Applicants have amended these claims to include the definitions of the variables D, P^1, R^1, R^4, $R^{4'}$, R^5, $R^{5'}$ and $R^{5''}$ as defined in the as-filed specification, for example, on page 47, lines 10-15; page 48, lines 1-6; and page 35, line 16, to page 36, line 22. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The Examiner rejects claim 42 as indefinite for allegedly being drawn to a method of using a compound of the general formula I or II, but depicting a specific formula that is not defined as formula I or II. Applicants have deleted the phrase "(I) or (II)" and respectfully request that this rejection be withdrawn.

Claim 44 is rejected as depending on withdrawn claims. Applicants have amended the claim to remove the dependencies to withdrawn claims. Therefore, this rejection is moot.

VI. Rejection Under 35 U.S.C. § 102

The Examiner rejects claims 1-5, 35, 44, and 50 under 35 U.S.C. § 102(b) as allegedly being anticipated by Filippini et al., "Can HCV affect the efficacy of anti-HIV treatment?" Archives of Virology, 145(5), 937-944, May 2000 ("Filippini"). Office Action at page 11. Applicants respectfully submit that Filippini is not § 102(b) prior art to the pending claims. The instant application was filed on October 18, 2001, but claims

priority to provisional application No. 60/241,488, filed October 18, 2000, and provisional application No. 60/282,156, filed April 6, 2001. In citing Filippini, the Examiner acknowledged that claims 1-5, 35, 44, and 50 "obtain the priority date of the provisional application 60/282,156 filed 4/6/2001." *Id.* at 11. The Table of Contents of volume 145, issue 5, of Archives of Virology identifies a publication date for that issue of May 15, 2000. M.P.E.P. § 707.05(f) instructs that "the publication date is the date of release when the material was made available to the public." Since this publication date is less than a year before Applicants' April 6, 2001, priority date, Filippini is not properly cited as § 102(b) prior art.

If the Examiner intended to assert Filippini as 35 U.S.C. § 102(a) art, Applicants submit that Filippini does not anticipate claims 1-5, 35, 44, and 50. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." M.P.E.P. § 2131 (quoting *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)) (emphasis added). Further, a rejection under § 102 is proper only when the claimed subject matter is identically described or disclosed in the prior art. *In re Arkley*, 455 F.2d 586, 587 (CCPA 1972) (emphasis added). The identical invention must be described in as complete detail as is contained in, and must be arranged as required by, the claim. M.P.E.P. § 2131.

Here, the Examiner asserts that "Filippini et al. disclose a method of treating patients with HCV compositions comprising Zalcitabine ..., which is known to be 2'-3'-dideoxycytidine." Office Action at page 11. Because 2'-3'-dideoxycytidine is a species of the rejected claims, the Examiner then alleges that "Filippini et al. inherently disclose

the methods as claimed, as they administer the same compound (Zalcitabine) to the same population, patients with HCV, and thus must have produced the same results." *Id.* Applicants respectfully disagree.

Applicants point out that zalcitabine was approved by the Food and Drug Administration to treat the human immunodeficiency virus (HIV). In their study, Filippini administered zalcitabine in combination with zidovudine, another antiretroviral nucleoside analog, and indinavir, an HIV-protease inhibitor, to a population of HIV and HCV co-infected patients and also to a second population infected with HIV only. Filippini at page 938. Filippini sought to evaluate the impact of new antiretroviral combinations on HCV viremia and also to evaluate the influence of HCV infection on the efficacy of the antiretroviral combinations administered. *Id.* Filippini concluded that none of the administered antiretroviral combinations were effective in treating HCV infection and that the response of HIV viral load to the antiretroviral combinations in patients with HIV/HCV coinfection was diminished. "While HCV-RNA levels were not affected by HAART [Highly Active Anti Retroviral Therapy], we noted an apparently diminished response of HIV viral load to this therapy in patients with HIV/HCV coinfection." *Id.* at 941. Thus, Filippini explicitly states that its method did not produce (inherently or otherwise) the same results as Applicants' method. In fact, Filippini's administered drug combination containing zalcitabine produced no effect on HCV-RNA levels. Applicants respectfully request that this rejection be withdrawn.

In addition, the Examiner rejects claims 1-5, 35-36, 39-42, 44, 50-51, and 54-57 under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent Application No. 2004/0110718 to Devos et al. ("Devos"). *See* Office Action at 11-12. Applicants

respectfully submit that Devos is not § 102(e) prior art to the pending claims. Devos was filed on October 3, 2003, as a continuation of U.S. Patent Application No. 09/923,620, filed on Aug. 7, 2001, now abandoned. Therefore, the effective U.S. filing date of Devos is August 7, 2001. The instant application was filed on October 18, 2001, but claims priority to provisional application No. 60/241,488, filed October 18, 2000, and provisional application No. 60/282,156, filed April 6, 2001. As discussed above, the Examiner has already acknowledged that claims 1-5, 35, 44, and 50 "obtain the priority date of the provisional application 60/282,156 filed 4/6/2001." *Id.* at 11. Likewise, since all of the claims of the instant application are supported by at least provisional application No. 60/282,156, the instant application is entitled to at least a priority date of April 6, 2001. Since the priority date of the instant application is before the § 102(e) date of Devos, Devos cannot be properly cited as § 102(e) prior art. Accordingly, Applicants respectfully request that this rejection be withdrawn.

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: July 3, 2007

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